REMARKS

Claims 26, 27 and 29-36 are currently pending and under consideration in the above-identified application.

REJECTION UNDER 35 U.S.C. § 103(a)

Claims 26, 27 and 29-36 remain rejected under 35 U.S.C. § 103(a), allegedly, as obvious over U.S. Patent No. 5,686,432 to Baggio et al. ("Baggio") in combination with U.S. Patent No. 5,252,339 to Cristofori et al. ("Cristofori") and U.S. Patent No. 5,496,807 to Marchi ("Marchi") for reasons of record. Applicants respectfully disagree with the rejection and the Examiner's reasoning for the rejection.

Although the Examiner is correct in stating on page 3 of the current office action that one cannot show nonobviousness by attacking references individually where the rejection is based on a combination of the references, Applicants point out that the cited references, especially Baggio, do not teach what the Examiner alleges they teach. For example, the Examiner specifically alleges on page 5 of the current office action that Baggio teaches dosages of sulodexide up to 500 mg. Applicants respectfully submit that Baggio does not teach dosages of up to 500 mg for sulodexide. Further, Baggio does not teach the treatment of renal insufficiency.

Baggio is directed to the use of glycosaminoglycans, including sulodexide, for treating the structural and functional degradation of the peritoneal membrane in patients with renal insufficiency, such as diabetic nephropathy. Baggio states in column 2, lines 36-44 that the "therapeutically effective dosages for this treatment depend on both the glycosaminoglycan used and the kind of patient and can vary between a minimum of 20 and a maximum of 500 mg a day." Applicants submit that this passage does not teach or even suggest that sulodexide can be administered at dosages up to 500 mg a day. The passage

specifically states that the dosage depends on the type of glycosaminoglycan used. The passage does not state that the dosage range of sulodexide is 20 to 500 mg a day. However, Baggio does teach in column 2, line 54, that sulodexide at a dosage of 50 mg can be used. Further in Example 4, the details of which are found in columns 5 and 6, Baggio administered only 50 mg a day to the human patient. Thus, Baggio, when read in its entirety as required (see, *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983)), clearly does not teach that sulodexide can be administered at a dosage of up to 500 mg a day. Rather, Baggio teaches that the dosage of the glycosaminoglycan depends on the type of glycosaminoglycan and states, in the specific case of sulodexide, that the dosage is 50 mg a day.

Further, with regard to the Examiner's statement that there is overlap between patients having diabetic nephropathy and patients having renal insufficiency, Applicants note that the passages in Baggio to which the Examiner recites are passages which refer to the teachings of European Patent Publication No. EP 0624374. This European Patent Publication is the European counterpart to Marchi. Thus, the teaching in Baggio quoted by the Examiner is nothing more than redundant of the teaching found in Marchi, and deals with the treatment of diabetic nephropathy with low doses of sulodexide. Applicants have always agreed that Marchi teaches the use of sulodexide for treating diabetic nephropathy, but only at certain low dosages, not at the dosages claimed in the present application.

Further, Applicants disagree with the Examiner's allegation that there is overlap in the patient populations. Although both patient populations suffer from renal insufficiency, the Examiner is pointing to a similarity that does not having any bearing on the claimed invention. Baggio treats the peritoneal membrane, not the kidney. As explained in Baggio in the background section as well in Applicants' previous response dated March 9, 2004, patients suffering from renal insufficiency can undergo a treatment of peritoneal

dialysis. However, this treatment results in damage to the peritoneal membrane, as evidenced, *e.g.*, by increased protein loss. Thus, this damage is not due to the fact that the patient has renal insufficiency, but, rather, to the treatment of peritoneal dialysis. Baggio teaches that the intraperitoneal administration of a glycosaminoglycan, such as sulodexide at 50 mg a day, can slow or reverse the damage to the peritoneal membrane. However, no effect is observed on the underlying renal insufficiency. Moreover, there is no evidence that the glycosaminoglycan as administered by Baggio even reaches the kidney since the intraperitoneal route of administration would not normally allow sulodexide to get into the blood stream. Thus, the Examiner's allegation that Baggio teaches the treatment of renal insufficiency, respectfully, is incorrect.

Thus, contrary to the Examiner's specific allegations, Baggio does not teach that sulodexide can be administered at a dosage of up to 500 mg a day and Baggio does not teach the treatment of diabetic nephropathy, but, rather, teaches the treatment of damage to the peritoneal membrane. Applicants emphasize to the Examiner that they are not simply attacking Baggio individually, but pointing out the fact that Baggio does not actually teach what the Examiner alleges Baggio teaches.

With regard to Marchi, Marchi does not teach a method for treating diabetic nephropathy by administering more than 150 mg sulodexide per day. In fact, Marchi administered only either (a) two capsules containing 250 LRU (25 mg) twice a day (column 3, lines 10-16 and column 4, lines 24-26 of Marchi); or (b) an injection of 600 LRU (60 mg) once a day (column 3, lines 35-40). Further, Marchi only provides evidence from clinical trials where the amounts of sulodexide administered are approximately one-fourth of the minimal amount taught and claimed in the present application.

Cristofori teaches the oral administration of sulodexide but for a completely different reason, *i.e.*, the "prevention and treatment of thrombotic and atherosclerotic

pathologies" (column 2, lines 50-51) and that administration of sulodexide is in such manner for "best performance of the anticoagulant, fibrinolitic antithrombotic, antitherosclerotic and antihyperlipoproteineic activities" (column 2, lines 55-58). Cristofori is completely silent as regards diabetic nephropathy. Since the claimed invention is directed to treating diabetic nephropathy, Cristofori is completely irrelevant to the claimed invention. Applicants do not understand the Examiner's reasoning for citing Cristofori.

Thus, the Examiner's concluding paragraph on page 5 of the current office action, which recites that "Baggio teaches dosages of up to 500 mg of sulodexide, which is taught in the prior art as being suitable for oral administration, for the treatment of renal insufficiency [diabetic nephropathy]" is, respectfully, incorrect since Baggio does not teach dosages of sulodexide of up to 500 mg per day and Baggio does not teach the treatment of renal insufficiency. Marchi and Cristofori do not fill in the gap between Baggio and the claimed invention in that the teachings of the cited references, alone or in combination, do not suggest the treatment of diabetic nephropathy with an effective dosage of sulodexide of at least 200 mg per day that does not cause adverse side effects. Applicants respectfully submit that the Examiner has failed to make a *prima facie* case for obviousness.

Therefore, in view of the foregoing, Applicants respectfully submit that the Section 103 rejection is improper, and thus, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants respectfully request that the remarks of the present response be entered and made of record in the present application. Claims 26, 27 and 29-36 fully meet all statutory requirements for patentability. Withdrawal of the Examiner's rejection and allowance and action for issuance are respectfully requested.

Applicants request that the Examiner call the undersigned at (212) 326-3921 if any questions or issues remain.

Respectfully submitted,

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Enclosures